# MATERIAL SAFETY DATA SHEET



## 1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

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## Material Name: Spironolactone and Furosemide Capsules

**Trade Name:** ALDALIX
**Chemical Family:** Mixture
**Intended Use:** Pharmaceutical product used as antihypertensive, diuretic

## 2. HAZARDS IDENTIFICATION

**Appearance:** Yellow Capsules
**Signal Word:** DANGER

**Statement of Hazard:**
May damage fertility or the unborn child.
Suspected of causing cancer.
May cause damage to: blood and blood forming organs through prolonged or repeated exposure.

**Additional Hazard Information:**

**Short Term:** Antihypertensive drug: has blood pressure-lowering properties

**Long Term:** Repeat-dose studies in animals have shown a potential to cause adverse effects on blood, kidneys, reproductive system.

**Known Clinical Effects:** Signs and symptoms might include nausea, vomiting, cramps, dizziness, headache, vertigo, low blood pressure on standing, rash, urticaria, photosensitivity, electrolyte imbalance, muscle spasm, weakness, and restlessness. Hypersensitivity reactions may also occur in susceptible individuals. Effects on blood and blood-forming organs have also occurred. May cause adverse effects on the developing fetus.

**EU Indication of danger:**
Harmful
Toxic to reproduction: Category 1
Carcinogenic: Category 3

**EU Hazard Symbols:**

T

**EU Risk Phrases:**

## 2. HAZARDS IDENTIFICATION

R40 - Limited evidence of a carcinogenic effect
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

**Note:** This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

## 3. COMPOSITION/INFORMATION ON INGREDIENTS

**Hazardous**

| Ingredient | CAS Number | EU EINECS/ELINCS List | Classification | % |
|---|---|---|---|---|
| Spironolactone | 52-01-7 | 200-133-6 | Repr.Cat.2;R60 Carc.Cat3;R40 Xn;R48/22 | 21 |
| Magnesium stearate | 557-04-0 | 209-150-3 | Not Listed | * |
| Furosemide | 54-31-9 | 200-203-6 | Not Listed | 8.3 |
| Corn Starch | 9005-25-8 | 232-679-6 | Not Listed | * |

| Ingredient | CAS Number | EU EINECS/ELINCS List | Classification | % |
|---|---|---|---|---|
| Lactose Monohydrate | 64044-51-5 | Not listed | Not Listed | * |
| Croscarmellose sodium | 74811-65-7 | Not listed | Not Listed | * |

**Additional Information:** Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

**For the full text of the R phrases mentioned in this Section, see Section 16**

## 4. FIRST AID MEASURES

**Eye Contact:** Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

**Skin Contact:** Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

**Ingestion:** Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

**Inhalation:** Remove to fresh air and keep patient at rest. Seek medical attention immediately.

**Symptoms and Effects of Exposure:** For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

## 5. FIRE FIGHTING MEASURES

**Extinguishing Media:** Use carbon dioxide, dry chemical, or water spray.

**Hazardous Combustion Products:** Toxic or corrosive gases including oxides of carbon and oxides of sulfur

**Fire Fighting Procedures:** During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

**Fire / Explosion Hazards:** Not applicable

## 6. ACCIDENTAL RELEASE MEASURES

**Health and Safety Precautions:** Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

**Measures for Cleaning / Collecting:** Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

**Measures for Environmental Protections:** Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

**Additional Consideration for Large Spills:** Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

## 7. HANDLING AND STORAGE

**General Handling:** Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8).

**Storage Conditions:** Store as directed by product packaging.

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Refer to available public information for specific member state Occupational Exposure Limits.**

**Spironolactone**

| | | |
|---|---|---|
| **Pfizer OEL TWA-8 Hr:** | 90 µg/m$^3$, Skin | |

**Magnesium stearate**

| | | |
|---|---|---|
| **ACGIH Threshold Limit Value (TWA)** | = 10 mg/m$^3$ TWA | except stearates of toxic metals |
| **Australia TWA** | = 10 mg/m$^3$ TWA | |
| **Belgium OEL - TWA** | Listed | |
| **Ireland OEL - TWAs** | = 10 mg/m$^3$ TWA | except lead stearate |
| **Lithuania OEL - TWA** | Listed | |
| **Portugal OEL - TWA** | Listed | |
| **Spain OEL - TWA** | Listed | |
| **Sweden OEL - TWAs** | = 5 mg/m$^3$ LLV | |

**Corn Starch**

| | | |
|---|---|---|
| **ACGIH Threshold Limit Value (TWA)** | = 10 mg/m$^3$ TWA | |
| **Australia TWA** | = 10 mg/m$^3$ TWA | |
| **Belgium OEL - TWA** | Listed | |
| **Bulgaria OEL - TWA** | Listed | |
| **Czech Republic OEL - TWA** | Listed | |
| **Greece OEL - TWA** | Listed | |
| **Ireland OEL - TWAs** | = 10 mg/m$^3$ TWA<br>= 4 mg/m$^3$ TWA | |
| **OSHA - Final PELS - TWAs:** | = 15 mg/m$^3$ TWA<br>= 5 mg/m$^3$ TWA | total |
| **Portugal OEL - TWA** | Listed | |
| **Spain OEL - TWA** | Listed | |

The exposure limit(s) listed for solid components are only relevant if dust may be generated.

**Engineering Controls:** General room ventilation is adequate unless the process generates dust, mist or fumes. Engineering controls should be used as the primary means to control exposures. Keep airborne contamination levels below the exposure limits listed above in this section.

**Environmental Exposure Controls:** Refer to specific Member State legislation for requirements under Community environmental legislation.

**Personal Protective Equipment:** Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

**Hands:** Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

**Eyes:** Wear safety glasses or goggles if eye contact is possible.

**Skin:** Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

**Respiratory protection:** If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

## 9. PHYSICAL AND CHEMICAL PROPERTIES:

| | | | |
|---|---|---|---|
| **Physical State:** | Capsule | **Color:** | Yellow |
| **Molecular Formula:** | Mixture | **Molecular Weight:** | Mixture |

## 9. PHYSICAL AND CHEMICAL PROPERTIES:

## 10. STABILITY AND REACTIVITY

**Stability:** Stable under normal conditions of use.
**Conditions to Avoid:** None known
**Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers

## 11. TOXICOLOGICAL INFORMATION

**General Information:** The information included in this section describes the potential hazards of the individual ingredients.

**Acute Toxicity: (Species, Route, End Point, Dose)**

**Spironolactone**
Rat Oral LD 50 4121 mg/kg
Mouse Oral LD 50 >1000mg/kg
Rabbit Oral LD 50 >1000mg/kg
Rat Intraperitoneal LD 50 786mg/kg

**Magnesium stearate**
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000mg/$m^3$

**Furosemide**
Rat Oral LD 50 2600 mg/kg
Mouse Intraperitoneal Minimum Symptomatic Dose 400mg/kg

**Lactose Monohydrate**
Rat Oral LD 50 29700 mg/kg

**Acute Toxicity Comments:** A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

**Irritation / Sensitization: (Study Type, Species, Severity)**

**Spironolactone**
Skin Sensitization - GPMT Guinea Pig No effect

**Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)**

**Spironolactone**
13 Week(s) Rat Oral 50 mg/kg LOAEL Blood
78 Week(s) Rat Oral 50 mg/kg/day LOAEL Liver Male reproductive system

**Furosemide**
13 Week(s) Rat Oral 300 mg/kg LOAEL
13 Week(s) Mouse Oral 600 mg/kg LOAEL
6 Month(s) Dog Oral 10 mg/kg/day LOAEL
2 Year(s) Rat Oral 30 mg/kg/day LOAEL

**Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))**

**Spironolactone**
Reproductive & Fertility Rat Oral 15 mg/kg/day NOAEL Fetotoxicity
Reproductive & Fertility Rat Intraperitoneal 100 mg/kg/day LOAEL Fertility
Embryo / Fetal Development Mouse Intraperitoneal 100 mg/kg/day LOAEL Maternal Toxicity
Embryo / Fetal Development Rat Oral 50 mg/kg/day LOAEL Fetotoxicity
Embryo / Fetal Development Rabbit Oral 20 mg/kg/day LOAEL Fetotoxicity

**Furosemide**
Reproductive & Fertility Rat Oral 2.9 mg/kg/day LOAEL Fertility

## 11. TOXICOLOGICAL INFORMATION

Embryo / Fetal Development Rabbit Oral 25 mg/kg LOAEL Maternal Toxicity, Fetotoxicity
Embryo / Fetal Development Rat Oral 12.5 mg/kg/day LOAEL Teratogenic
Embryo / Fetal Development Mouse Oral 1250 mg/kg/day LOAEL Fetotoxicity, Teratogenic

**Genetic Toxicity: (Study Type, Cell Type/Organism, Result)**

**Spironolactone**
Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative
Mammalian Cell Mutagenicity Negative without activation

**Furosemide**
Bacterial Mutagenicity (Ames) Negative
*In Vitro* Micronucleus Human Lymphocytes Positive
Mammalian Cell Mutagenicity Mouse Lymphoma Positive

**Lactose Monohydrate**
*In Vitro* Bacterial Mutagenicity (Ames) Negative

**Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))**

**Spironolactone**
104 Week(s) Rat Oral 10 mg/kg/day LOAEL Benign tumors
52 Week(s) Non-human Primate Oral 20 mg/kg/day LOAEL Reproductive System

**Carcinogen Status:** See below

**Spironolactone**
**IARC:** Group 3 (Not Classifiable)

**Furosemide**
**IARC:** Group 3 (Not Classifiable)

## 12. ECOLOGICAL INFORMATION

**Environmental Overview:** Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

## 13. DISPOSAL CONSIDERATIONS

**Disposal Procedures:** Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

## 14. TRANSPORT INFORMATION

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

## 15. REGULATORY INFORMATION

**EU Symbol:** T
**EU Indication of danger:** Harmful
Toxic to reproduction: Category 1
Carcinogenic: Category 3

**EU Risk Phrases:**

R40 - Limited evidence of a carcinogenic effect
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

**EU Safety Phrases:**

S22 - Do not breathe dust.
S24 - Avoid contact with skin.
S53 - Avoid exposure - obtain special instructions before use.

**OSHA Label:**
DANGER
May damage fertility or the unborn child.
Suspected of causing cancer.
May cause damage to: blood and blood forming organs through prolonged or repeated exposure.

**Canada - WHMIS: Classifications**

**WHMIS hazard class:**
Class D, Division 2, Subdivision A

**Spironolactone**

| | |
|---|---|
| **California Proposition 65** | carcinogen, initial date 5/1/97 |
| **Inventory - United States TSCA - Sect. 8(b)** | Present |
| **Australia (AICS):** | Present |
| **Standard for the Uniform Scheduling for Drugs and Poisons:** | Schedule 4 |
| **EU EINECS/ELINCS List** | 200-133-6 |

**Magnesium stearate**

| | |
|---|---|
| **Inventory - United States TSCA - Sect. 8(b)** | Present |
| **Australia (AICS):** | Present |
| **EU EINECS/ELINCS List** | 209-150-3 |

**Furosemide**

| | |
|---|---|
| **Australia (AICS):** | Present |
| **Standard for the Uniform Scheduling for Drugs and Poisons:** | Schedule 4 |

## 15. REGULATORY INFORMATION

| | |
|---|---|
| **EU EINECS/ELINCS List** | 200-203-6 |

**Corn Starch**

| | |
|---|---|
| **Inventory - United States TSCA - Sect. 8(b)** | XU |
| **Australia (AICS):** | Present |
| **REACH - Annex IV - Exemptions from the obligations of Register:** | Present |
| **EU EINECS/ELINCS List** | 232-679-6 |

**Lactose Monohydrate**

| | |
|---|---|
| **Australia (AICS):** | Present |

**Croscarmellose sodium**

| | |
|---|---|
| **Australia (AICS):** | Present |

## 16. OTHER INFORMATION

**Text of R phrases mentioned in Section 3**

R40 - Limited evidence of a carcinogenic effect
R60 - May impair fertility.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.

**Data Sources:** Safety data sheets for individual ingredients. The data contained in this MSDS may have been gathered from confidential internal sources, raw material suppliers, or from the published literature.

**Prepared by:** Corporate Occupational Toxicology & Hazard Assessment

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

**End of Safety Data Sheet**